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TITLE: Biological Approaches to Prevent the Sexual Transmission of HIV

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BACKGROUND: Sexual transmission of HIV results from the infectiousness of the host and the susceptibility of the index case. Infectiousness most likely reflects the size of the inoculum in the genital secretions, and the phenotype of the viral variants found in these secretions.

METHODS: Particular HIV variants are selected for transmission based on unique envelope sequences, which confer the "NSI" phenotype. Susceptibility to infection depends on the number of cells expressing CD4 and CCR5 receptors, and the number of receptors/cell. Both acquired and hereditary resistance to infection have been reported. US HIV prevention strategies have focused primarily on reducing susceptibility, while reducing infectiousness may ultimately prove a more realistic goal.

RESULTS: While the concentration of HIV in seminal plasma correlated with the blood viral burden, several lines of evidence demonstrate that HIV undergoes independent replication in the genital tract. HIV variants recovered from blood and semen are not always identical. Therefore, biological strategies to reduce infectiousness of HIV must be directed at genital tract replication. STDs that cause mucosal inflammation (gonorrhea, chlamydia and trichomonas) greatly increase the concentration of HIV in seminal plasma and the ease of detection of HIV in female genital secretions. These increases can be reversed with antibacterial therapy. Conversely, antiretroviral therapy produces sustained reduction of excretion of HIV in semen, and reflect penetration of antiretroviral drugs into seminal plasma.

CONCLUSIONS: The epidemiology of HIV transmission strongly suggests that the concentration of virus in semen predicts the efficiency of sexual transmission. Strategies designed to reduce excretion of HIV in genital secretions are likely to prevent transmission.

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